

SPINAL STENOSIS WITH PARAPARESIS IN A KOREAN BOY WITH ALBRIGHT'S HEREDITARY OSTEODYSTROPHY : A NOVEL MUTATION OF GNAS GENE

Ji Eun Lee ¹⁾, Sang Heon Lee ¹⁾, Sung Yoon Cho ²⁾, Dong-Kyu Jin ²⁾, Chang-Seok Ki ³⁾

¹⁾ Department of Pediatrics, Graduate School of Medicine, Inha University of Medicine, Inha University Hospital, Incheon, Republic of Korea

²⁾ Department of Pediatrics, Sungkyunkwan University School of Medicine, Seoul, Republic of Korea

³⁾ Department of Laboratory Medicine and Genetics, Sungkyunkwan University School of Medicine, Seoul, Republic of Korea

INTRODUCTION

Spinal stenosis and compressive myelopathy was rarely reported among Albright's hereditary osteodystrophy (AHO) patients, mainly adults. The association of symptomatic spinal stenosis with AHO is not well known. We presented a Korean boy with AHO features and delayed diagnosis of PHP-Ia, suffering from cervical spinal stenosis and paraparesis, having a novel *GNAS* mutation, while his mother had PPHP with AHO phenotype of the same novel gene mutation.

MATERIAL & METHODS

A 15-year-old boy was referred to the pediatric clinic at our hospital for asthma induced dyspnea. He had a history of developmental delay and moderate cognitive impairment (Intelligence Quotient 45) without any history of seizure or tetany. At the age of 13, he underwent trans-anal Soave surgery for Hirschsprung disease which was later diagnosed. At the age of 14, he had developed progressive weakness in both lower extremities after several falls, and spine MRI revealed multi-level congenital cervical spinal stenosis and compressive myelopathy at C3-5 level (Fig.1.). After 4 months, he underwent decompressive cervical laminoplasty due to progressive spastic paraplegia.

At 2 months postoperatively, he was wheelchair-bound with residual weakness and partial improvement in strength. Physical examination showed short stature (140cm, -6.7 SDS) and typical somatic features of AHO including round face, poorly arranged teeth, brachydactyly of hands and feet, short neck. The patient's mother had typical AHO features and short stature (150cm, -2 SDS), central obesity (weight 65kg, BMI 29.3), and mild mental retardation, but did not show any laboratory evidence of hormone resistance and abnormal radiographic finding.

	Age (yr)	CA (mg/dl)	P (mg/dL)	PTH (pg/ml)	ALP (IU/L)	25-OH Vit. D ₃ (ng/dl)
Patient	15	7.7	5.9	339.69	727	13
Mother	43	9.0	4.2	45.50	208	28

Fig.1. T2- weighted sagittal (A) and axial (B) images of MRI of cervical spine showed multiple stenosis of central canal caused by multiple bulging discs and narrowed AP diameter of central canal

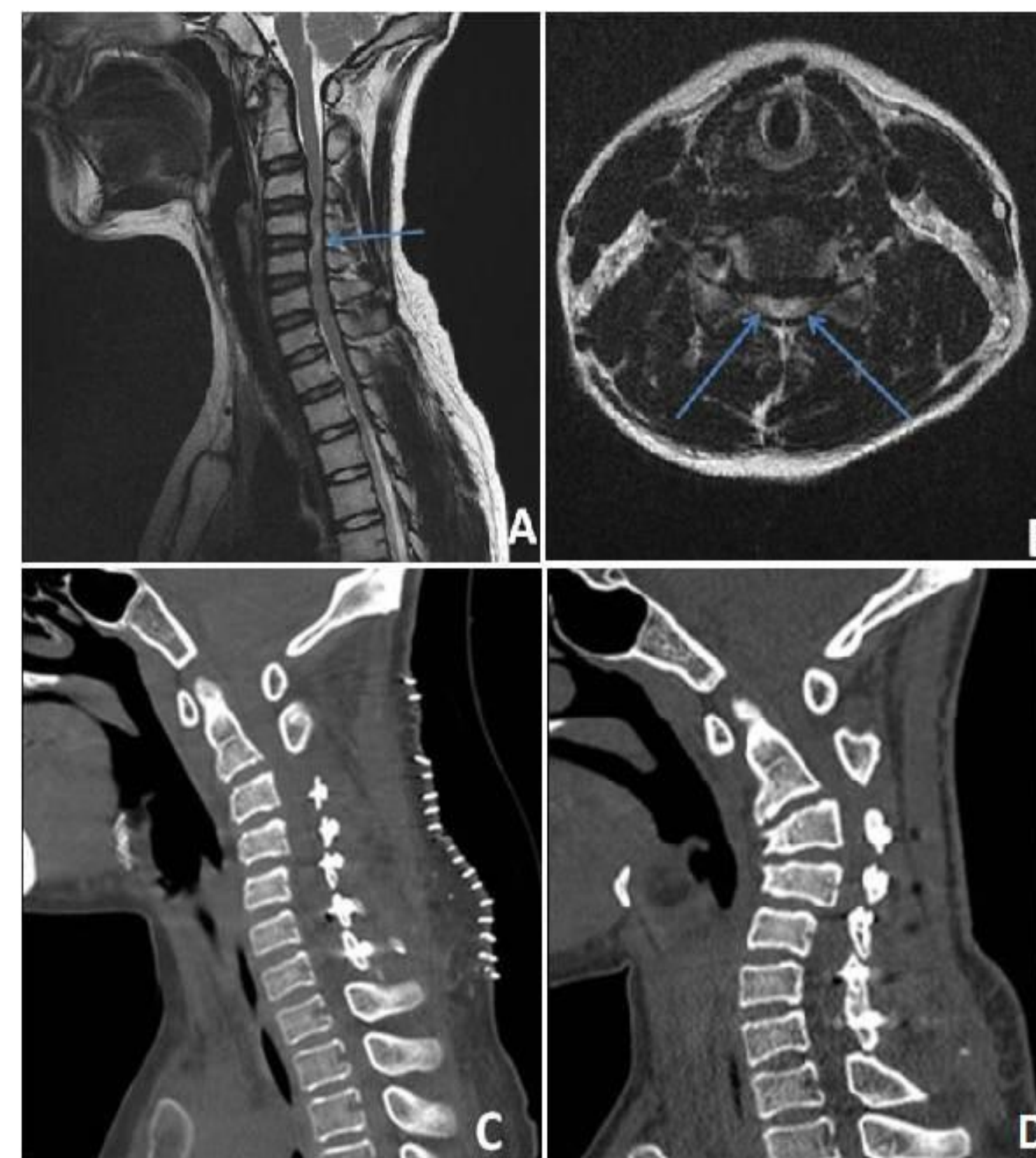
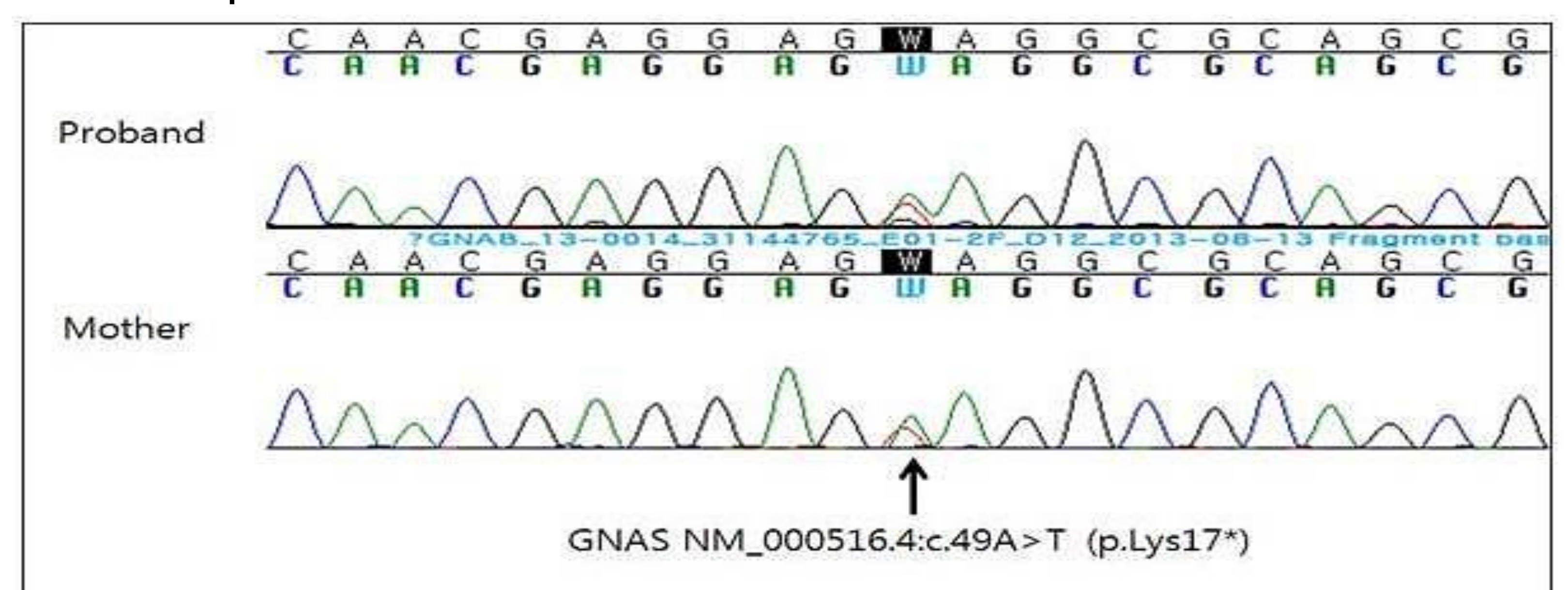


Fig.2. Patient was wheelchair-bound and his mother was standing beside him.

GENETIC ANALYSIS

We performed *GNAS* gene analysis. All of exons and adjacent intronic region of *GNAS* gene were amplified by PCR. Cycle sequencing analysis was performed using the BigDye Terminator Cycle Sequencing Ready Reaction kit.

The heterozygous nonsense mutation in exon 1 of the *GNAS* gene, *GNAS* NM_000516.4:c.49A>T (p.Lys17*), was identified in both the patient and his mother.



CONCLUSIONS

This is the first clinically, biochemically and genetically identified child case of spinal stenosis and paraparesis associated with PHP-Ia, having a novel *GNAS* mutation in Korea.

Reference

1. *Pediatr Neurosurg*2008;44:337
2. *J. Endocrinol. Invest.* 2005;28: 646